201-14676

NCIC HPV
Sent by: Mary-Beth Weaver

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To: NCIC HPV, moran.matthew@epa.gov
cc:
cc:
Subject: Environmental Defense comments on the Mononitroaniline Category

Richard_Denison@environmentaldefense.org on 08/15/2003 06:11:36 PM

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Subject: Environmental Defense comments on the Mononitroaniline Category

(Submitted via Internet 8/15/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and frjoha@solutia.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for the Mononitroaniline Category.

The test plan on the proposed mononitroaniline category was prepared by Solutia Inc. The category is comprised of two members; 2-nitroaniline (ONA) (CAS# 88-74-4) and 4-nitroaniline (PNA) (CAS # 100-01-6). The category is well-justified and limited use of read-across for HPV endpoints is proposed, so we agree with the proposed category. Also, we agree with the sponsor that no additional tests are needed to fulfill HPV screening level requirements.

The sponsor states that both mononitroanilines are manufactured at a single site in the U.S. in "an essentially closed, continuous process." They are sold to customers at a few U.S. sites, according to the sponsor, where they are used exclusively in the synthesis of numerous industrial chemicals. The sponsor states that there are no known direct commercial uses for the mononitroanilines and they are fully consumed as chemical intermediates. Opportunities for environmental releases and human exposures appear to be greatest during transport and during its use as a chemical intermediate.

The test plan and robust summaries are complete, well organized and informative. Specific comments are as follows:

1. Repeat dose studies are available for PNA including a 90-day oral study but only 28-day inhalation studies are available for ONA. These studies indicate that methemoglobinemia and associated clinical parameters are the hallmark effects of both ONA and PNA. PNA appears to be somewhat more potent than ONA in cases where data are comparable. One of the ONA repeat dose studies detected testicular effects, but this finding was shown to be caused by ethylene glycol monoethyl ether (EGME), a known testicular toxicant, used in the generation of the inhalation exposure. A second study, using the same or higher doses without EGME, was negative for testicular toxicity. We agree that existing repeat dose studies are adequate for the repeat dose endpoint and that the mononitrolanilines do not appear to be testicular toxicants.

2. The sponsor claims that ONA and PNA have been shown to act through a common mode of action. While we agree that the category is justified, existing data only demonstrate a common pattern of toxic effects. No data were presented on the biological processes which cause those effects. For

example, no metabolism or gene expression data were presented in the test plan or robust summary. Although this category appears well-behaved, both metabolism and gene expression data could significantly increase confidence in the validity of this proposed category, and more generally.

3. There are no existing reproductive toxicity studies on ONA, although there are complete and well-done reproductive and developmental toxicity studies on PNA. We agree with the sponsor that a reproductive toxicity study is not needed on ONA because ONA has been studied for developmental toxicity, PNA appears to be more toxic than ONA, ONA is negative in genetic toxicity studies, no histological effects on the gonads are caused by ONA, and ONA is produced in a closed system.

Thank you for this opportunity to comment.

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